AMENDMENTS TO THE SPECIFICATION

On page 4, in the paragraph beginning on line 8, replace the paragraph with the following:

"Genomics services" as used herein means processes used to generate genomics products, for example and without limitation, gene cloning, customized DNA or polypeptide library production, gene expression, custom antibody libraries, transgenic animal production, amino and nucleic acid sequencing, etc. "Genomics product" as used herein means a physical product made as a result of performing genomics services. For example, and without limitation, a genomics product is a cloned nucleic acids-cDNA, a cloned gene, a cell line transfected with a cloned cDNA, gene or gene fragment, one or more cell lines with targeted modification(s) to an endogenous nucleic acid a gene, a library of proteins expressed by a plurality of endogenous nucleic acids each with at least one targeted modification, DNA primers, synthesized gene(s), custom DNA libraries, transgenic animals having a targeted modification to an endogenous nucleic acid or a knock-out of one or more endogenous alleles, the phenotype of modified cells or animals, database of genomic data, databases that correlate genotypic and phenotypic data, and biopharmaceuticals.

On page 4, in the paragraph beginning on line 21, replace the paragraph with the following:

Generally, a customer uses customer computer **12**, or other suitable communication device (such as a phone or facsimile; although a computer is preferred) to transmit a request over communications network [[14XX]] **14** to genomic services computer **16**. Communications network **14** is preferably the internet, an extranet or a combination of the two. It is understood that communications network **14** includes a public switched telephone network, satellite network or any other means for permitting the customer to transmit the request to genomics services computer **16**.

On page 5, in the paragraph beginning on line 17, replace the paragraph with the following:

Referring to FIG. 2, requests database **34** contains searchable entries, preferably with hierarchical access schemes to limit access to a particular customer's outstanding request(s) to the customer, and to selected individuals at DirectGenomics. Entries **40** of requests database **34** may include, without limitation, unique customer number **42**, unique order identification number **44**, sequence data **46** submitted with request, genomics product(s) and/or services ordered **48** with request, and status **50** of each genomics product(s) ordered. Referring to FIG. 3, reports database **38** also contains searchable entries with access limited to the customer providing the customer access to all previous orders and the reports therefore. Entries **52** of reports database may include, without limitation, unique customer number **42**, unique order identification number **44**, report **54** for each requested genomics product or service, time stamp **56**, and report status **56**. Report **54** includes data generated and reported from the requested genomics product, for example and without limitation, the nucleic acid sequence of a cloned gene, a protein sequence expressed by the gene, or the results of drug screens against [[agains]] cell lines expressing the cloned gene, etc.

On page 6, in the paragraph beginning on line 1, replace the paragraph with the following:

Referring to FIG. 4, genomic services database **36** includes searchable entries **60** to identify companies that provide a given service. Each entry may include the information provided in FIG. 4. Additionally, preferably each company is ranked based on the effectiveness with which it provides a given service. The rank may be based upon such criteria as timeliness, accuracy, expertise, or price. The rank provides [[proivdes]] one means by which the expertise of DirectGenomics [[DirctGenomics]] may be utilized in identifying from which company to obtain the genomics product or service, if DirectGenomics does not provide it. Preferably DirectGenomics will provide the requested product or service, and

would thus select itself. If DirectGenomics does not provide one or more of the services or products, the company rankings are used to select a provider. Alternatively, DirectGenomics may contract for specific products or services not provided by DirectGenomics from one company, such that the specific product or service, if requested, would always be provided by the one company. This provides the ability to obtain bulk discounts as well as access specialized expertise for that one specific product or service. The skilled artisan will recognize that other combinations may be used without exceeding the scope of the present invention.

On page 6, in the paragraph beginning on line 16, replace the paragraph with the following:

Referring to FIG. 5, request receiving application **28** begins with the customer accessing DirectGenomics website [[<http://www.directgenomics.com>]] and accessing customer order page. Customer order page contains general instructions on how to place an order for genomics products and/or services, fields and menus are provided for entering data and selecting criteria (*e.g.*, services and/or products) necessary for completing the order. For example, and without limitation, the following self-explanatory fields, buttons and menus are provided: customer identification number field and/or cookie therefor, nucleic acid sequence field and/or a pointer to a nucleic acid sequence (*e.g.*, a reference number in a database containing the sequence), pull down menu for selecting one or more (preferably at least two) genomics products, and comments field. After completing order page, the customer clicks the submit button which transmits the request to genomic services computer **16**.

On page 7, in the paragraph beginning on line 20, replace the paragraph with the following:

Next, the nucleic acid sequence, in this example an EST, is used to search the customers completed reports within the system, which are more fully described below, to determine if any related or redundant genomic products had been previously requested and [[produce]] <u>produced</u>. Additionally, request receiving application **28** can search the

customer's proprietary databases through a secured link to make the same determination. If there is a redundancy or similarity between work previously completed and the requested genomics products and/or the submitted EST then the program sends off a prescripted message to the customer to provide this additional information. Alternatively or in combination with the electronic message, an individual at DirectGenomics would be notified to contact the customer directly to discuss the additional information. If no redundancy exits (*i.e.*, no additional information is found), the EST sequence is used to search public and/or proprietary databases to determine if the one or more genes comprising the EST or something close thereto had been previously cloned. If so, the program sends off a prescripted message to the customer to provide this additional information.

One page 12, in the paragraph beginning on line 12, replace the paragraph with the following:

9. a recombinase mediated process, and at least one single-stranded targeting polynucleotide are used to generate transgenic mice having targeted [[modifiedendogenous]] <u>modified endogenous</u> nucleic acid; and

On page 14, in the paragraph beginning on line 19, replace the paragraph with the following:

Additionally, the process may be used to identify [[of]] functional domains, and validate the selected sequences. The high-throughput automated analysis of the gene clones (cDNAs, genomic DNA, alternative splice forms, polymorphisms, gene family members) will provide informative analysis of the qualitative differences between expressed genes (gene profiling). Sequence analysis of the isolated cDNAs and genomic DNA allows diagnostic testing for single and multiple nucleotide polymorphisms, loss of heterozygosity (LOH), and other chromosomal abnormalities. Differences in gene families and mRNA spliced isoforms can be elucidated, and information can be provided on the nature of the mRNA. Libraries of clones obtained at the end of the process will mimic the difference between normal and genetic

disorders (or between any differential event). These libraries can be used to screen for genetic signatures and the technology can elucidate precise potential domains of therapeutic intervention within coding sequences of the gene, including catalytic domains (ie, kinases, phosphatases, proteases), protein-protein interaction domains, truncated receptors and soluble receptors.

On page 21, in the paragraph beginning on line 25, replace the paragraph with the following:

This invention describes integrating many of the functional genomic services resulting in the benefits of economies of scale. Additionally, utilizing [[recobinase]] recombinase mediated processes further enhances the benefits of the stream lined integrated functional genomics services. More specifically the recombinase mediated processes specifically, efficiently and reliably target and isolate specific DNA molecules for applications such as DNA cloning; biovalidation of drug targets; DNA modification, including mutagenesis, gene shuffling and evolution; isolation of gene families, orthologs, and paralogs; identification of alternatively spliced isoforms; gene mapping; diagnostic testing for single and multiple nucleotide polymorphisms; differential gene expression and genetic profiling; nucleic acid library production, subtraction and normalization; in situ gene targeting (hybribidization) in cells; in situ gene recombination in cells and animals; high throughput phenotype screening of cells and animals; phenotyping small molecule compounds; screening for pharmaceutical drug regulators; and biovalidation of drugs in transgenic recombinant cells and animals.